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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/202,549	10/12/1999	PHILIP N. TSICHLIS	FCC 96-11	3050

7590 02/26/2003

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EXAMINER
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ART UNIT	PAPER NUMBER
2636	27

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding

Application No.	Applicant(s)
09/202,549	TSICHLIS ET AL
Examiner	**Art Unit**
David A Lambertson	1636

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2003*

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 August 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4)☐ Interview Summary (PTO-413) Paper No(s). *29*
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *See Continuation Sheet*

DETAILED ACTION

Receipt is acknowledged of a reply, filed November 29, 2002 as Paper No. 25, to the previous Office Action. Receipt is acknowledged of a reply, filed January 24, 2003 as Paper No. 27, to the previous interview, conducted January 23, 2003. Amendments were made to the claims, and claim 25 was cancelled

Claims 1-24 are pending in the instant application. Claims 12-20 were previously withdrawn from consideration, and remain so. Any rejection of record in the previous Office Action, Paper No. 18, mailed January 15, 2002, that is not addressed in this action has been withdrawn. Because new rejections are made herein that were not necessitated by applicant's amendment of the claims in Paper No. 25, this is NOT A FINAL ACTION.

Claims 1-11 and 21-24 are under consideration in the instant application.

Drawings

New corrected drawings are required in this application because of the reasons set forth in the attached Draftsperson's review, form PTO-948. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

Applicant is informed that the specification is not in sequence compliance. See the attached STIC Error Report for the reasons. Applicant is required to provide a substitute paper copy and computer readable form (CRF) of the sequence listing, a statement saying the two are the same, and a statement that no new matter has been entered as a result of the new sequence listing, after applicant has made the appropriate corrections.

Applicant is informed that the amendment to the specification concerning Table II, originally submitted on July 23, 2002 and again requested for submission on January 24, 2005, has not been entered for the following reason. The table as amended does not conform to the acceptable standards for a Table. Specifically, that Table extends over two pages. Applicant is required to submit Table II as a new drawing figure and provide a Brief Description of said drawing figure.

Claim Objections

Claim 6 is objected to because of the following informalities: claim 6 contains an abbreviation that is not first spelled out, specifically MIE (Major Immediate Early). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection not necessitated by applicant's amendment.**

Applicant claims a DNA construct comprising a mutated Gfi-1 binding site, where the binding site prior to mutation is greater than 65% (claim 7) or 79% (claim 8) homologous with the consensus binding sequence for Gfi-1. The claims read on a broad genus of sequences prior to mutation that are capable of binding Gfi-1 prior to mutation, but not after mutation.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims the sequences by function only, without any disclosed or known correlation between the elements and their function. The specification only provides a description concerning the binding of Gfi-1 to the consensus sequence prior to its mutation, and does not describe a representative number of sequences that are 65% or 79% homologous to the consensus sequence. The specification, although listing a number of potential Gfi-1 binding sites

in Table II of the instant specification, does not indicate that these sequences are actually Gfi-1 binding sites. Furthermore, there is no clear indication as to how to determine the degree of homology between the consensus sequence and a Gfi-1 binding sequence as claimed, especially in light of the variable nature of the consensus sequence (i.e., how does "N" affect the determination of homology). As a result, the skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification does not disclose what sequences that are 65% or 79% homologous to Gfi-1 are actually capable of binding to Gfi-1, and which therefore are subject to mutation in order to prevent the binding of Gfi-1.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the specification. There is no description in the prior art with regard to sequences that are 65% or 79% homologous with the consensus Gfi-1 binding site that are capable of binding to Gfi-1 prior to, but subsequent to, mutation. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art describes a representative number of Gfi-1 binding sites with 65% or 79% homology to the consensus site that are capable of binding to Gfi-1 prior to, but not subsequent to, mutation. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention

Claims 1-6, 10, 11, 23 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection not necessitated by applicant's amendment.**

Claims 1-6, 10, 11, 23 and 24 are indefinite because the metes and bounds of the claim are unclear. The claims are directed to a Gfi-1 binding site, which upon mutation is no longer capable of binding to Gfi-1. It is unclear if the claim is referring to the consensus binding site, or if it is referring to another binding site. Furthermore, because the binding site for Gfi-1 was determined by multiple methods, each giving a different result (e.g., DNA foot-printing gives a 21 bp overlap with a proposed 12 bp binding site, while DMS interference indicates a 9 bp binding sequence), the metes and bounds of "Gfi-1 binding site" are unclear. Also, it is unclear if the term encompasses binding sites by other methods that are not disclosed in the specification. Therefore, the starting material upon which the mutations are made is indefinite, and the claim is indefinite as a result.

Claim 24 recites the limitation "AATC" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim. The claim from which claim 24 depends does not indicate any sequences containing the tetranucleotide "AATC", therefore it is unclear what sequence is being referred to in claim 24.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-11 and 21-24 are rejected under 35 U.S.C. 102(a) as being anticipated by Zweidler-McKay *et al.* (IDS reference #4; henceforth Zweidler; published August 1996). **This is a new rejection not necessitated by applicant's amendment.**

Zweidler teaches the identification of a consensus Gfi-1 binding site, the mutation of the consensus binding site to determine residues that affect the binding of the Gfi-1 protein, the identification of a consensus Gfi-1 binding site in the human cytomegalovirus MIE promoter and expression constructs comprising the human cytomegalovirus MIE promoter (HCMV-MIE) wherein the Gfi-1 binding site has been mutated. Specifically, Zweidler identifies the consensus

binding site for Gfi-1 as being TAAATCACCA TGCA, where the underlined portion is an important motif (see for example Figure 3 and page 4027, the first full paragraph on the right side). Zweidler also establishes that mutation of the "AATC" motif abolishes the interaction with Gfi-1 (see figure 5 and page 4028, first full paragraph, left side). Zweidler demonstrates that Gfi-1 can bind to the HCMV-MIE promoter, where it represses the expression of a CAT-reporter gene; Zweidler also teaches that mutating the "AATC" site to "AACT" in the context of the HCMV-MIE promoter (as is done in the construct of SEQ ID NO: 14 of the instant application) results in alleviation of the Gfi-1-dependent repression/improved expression of CAT reporter gene expression (see for example Figure 7 and page 4029, second full paragraph, right side). Finally, Zweidler teaches that Gfi-1 binding sites are present in the promoters of proto-oncogenes, and therefore play a role in the inhibition of their expression (see for example the Abstract).

Claims 1-4 and 7-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Bang et al. (US Patent No. 4,992,373; see entire document; henceforth Bang). **This is a new rejection not necessitated by applicant's amendment.**

The claims read on a DNA construct that has a mutated Gfi-1 binding sequence, whereby binding by Gfi-1 is prohibited. Because mutation of the sequence is not limited by the definition provided by the specification (see page 4, lines 15-19), the mutation could, for example, comprise a complete deletion of the Gfi-1 binding sequence. Since a complete deletion of a Gfi-1 binding sequence is within the scope of the claims, the claim reads on any DNA construct that does not contain a Gfi-1 binding site, because the absence of such a site would be expected not

bind to Gfi-1. Applicant is reminded that the claims are drawn to the product, and not to a method of making the product, therefore the mutation event does not distinguish the claimed invention over the prior art cited below.

Bang discloses a DNA construct comprising a promoter that does not contain a Gfi-1 binding site (see for example column 19, lines 22-40), therefore the DNA construct does not have the capacity to bind Gfi-1 hence said binding is prevented. Since the vector is a viral vector (pSV2-type, an SV40 viral vector), the promoter sequence in the construct is necessarily a viral promoter sequence. The promoter is active in mammalian cells, dictated by the use of mammalian cells in conjunction with the vector (see for example column 18, lines 4-14). Finally, Bang describes the use of the vector comprised of a promoter lacking a Gfi-1 binding site to produce protein C (a plasma protein; i.e. a growth factor), wherein the protein C sequence is operatively linked to the promoter (see for example column 11, line 65 to column 12, line 20). As such, Bang anticipates the claims set forth in the instant application.

Claims 1-4 and 7-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Eglitis et al. (US Patent No. 5,672,510; see entire document; henceforth Eglitis). **This is a new rejection not necessitated by applicant's amendment.**

The claims read on a DNA construct that has a mutated Gfi-1 binding sequence, whereby binding by Gfi-1 is prohibited. Because mutation of the sequence is not limited by the definition provided by the specification (see page 4, lines 15-19), the mutation could, for example, comprise a complete deletion of the Gfi-1 binding sequence. Since a complete deletion of a Gfi-1 binding sequence is within the scope of the claims, the claim reads on any DNA construct that

does not contain a Gfi-1 binding site, because the absence of such a site would be expected not bind to Gfi-1. Applicant is reminded that the claims are drawn to the product, and not to a method of making the product, therefore the mutation event does not distinguish the claimed invention over the prior art cited below.

Eglitis discloses a DNA sequence comprising a promoter that does not contain a Gfi-1 binding site (see for example column 4, lines 6-53), therefore the DNA construct does not have the capacity to bind Gfi-1 hence said binding is prevented. Since the vector is a retroviral vector (e.g., a Maloney Murine Lukemia Virus vector; see for example column 4, lines 48-50), the promoter sequence in the construct is necessarily a viral promoter sequence that is functional in mammalian cells. Eglitis also teaches the expression of interleukins, growth factors, etc. that are operably linked to the promoter sequence lacking a Gfi-1 binding site (see for example column 2, lines 31-40, column 8 line 62 to column 9, line 2, and claim 24). As such, Eglitis anticipates the claims set forth in the instant application.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph D, can be reached on (703) 305-1998. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
February 24, 2003

Gerald G. Hoffers Jr
PATENT EXAMINER
A.U. 1636